



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2017-N-5925]

21st Century Cures Act: Annual Compilation of Notices of Updates from the Susceptibility Test Interpretive Criteria Web Page; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for comments.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is announcing the availability of the Agency's annual compilation of notices of updates to the Agency's Susceptibility Test Interpretive Criteria web page. The Agency established the Susceptibility Test Interpretive Criteria web page on December 13, 2017, and since establishment has provided updates to both the format of the web pages and to the susceptibility test interpretive criteria identified and recognized by FDA on the web pages. FDA is publishing this notice in accordance with procedures established by the 21st Century Cures Act (Cures Act).

DATES: This notice is published in the *Federal Register* on [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: You may submit either electronic or written comments and information as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including

attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2017-N-5925 for "Susceptibility Test Interpretive Criteria Recognized and Listed on the Susceptibility Test Interpretive Web Page; Request for Comments." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at

<https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the

prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Katherine Schumann, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 6242, Silver Spring, MD 20993-0002, 301-796-1182, Katherine.Schumann@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

Section 511A of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 360a-2), as added by section 3044 of the Cures Act (Pub. L. 114-255), was signed into law on December 13, 2016. This provision clarifies FDA's authority to identify and efficiently update susceptibility test interpretive criteria, including through the recognition by FDA of standards established by standards development organizations (SDOs). It also clarifies that sponsors of antimicrobial susceptibility testing devices may rely upon listed susceptibility test interpretive criteria to support premarket authorization of their devices, provided they meet certain conditions, which allows for a more streamlined process for incorporating up-to-date information into such devices.

In the *Federal Register* notice of December 13, 2017 (82 FR 58617), FDA announced the establishment of the Susceptibility Test Interpretive Criteria web page. This web page recognizes susceptibility test interpretive criteria established by an SDO that fulfills the requirements under section 511A(b)(2)(A) of the FD&C Act; identifies when FDA does not recognize, in whole or in part, susceptibility test interpretive criteria established by an SDO; and lists susceptibility test interpretive criteria identified by FDA outside the SDO process. The susceptibility test interpretive criteria listed by FDA on the Susceptibility Test Interpretive

Criteria web page is deemed to be recognized as a standard under section 514(c)(1) of the FD&C Act (21 U.S.C. 360d(c)(1)). The Susceptibility Test Interpretive Criteria web page can be found at <https://www.fda.gov/STIC>.

On March 1, 2018, FDA published a notice in the *Federal Register* (83 FR 8883) requesting comments on FDA's initial susceptibility test interpretive criteria recognition and listing determinations on the Susceptibility Test Interpretive Criteria web page (<https://www.federalregister.gov/documents/2018/03/01/2018-04175/susceptibility-test-interpretive-criteria-recognized-and-listed-on-the-susceptibility-test>). FDA may consider information provided by interested third parties as a basis for evaluating new or updated interpretive criteria standards (section 511A(c)(2)(B) of the FD&C Act); third parties should submit any information they wish to convey to the Agency to Docket No. FDA-2017-N-5925. If comments are received, FDA will review those comments and will make, as appropriate, updates to the recognized standards or susceptibility test interpretive criteria.

At least every 6 months after the establishment of the Susceptibility Test Interpretive Criteria web page, FDA is required, as appropriate to: (1) publish on that web page a notice recognizing new or updated susceptibility test interpretive criteria standards, or recognizing or declining to recognize parts of standards; (2) withdraw recognition of susceptibility test interpretive criteria standards, or parts of standards; and (3) make any other necessary updates to the lists published on the Susceptibility Test Interpretive Criteria web page (section 511A(c)(1)(A) of the FD&C Act). FDA has provided notices of updates on the Susceptibility Test Interpretive Criteria web page, which can be found here: <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm593952.htm>. Interested parties may also sign up to receive emails informing them of these updates as they

occur by using the link provided either on the main Susceptibility Test Interpretive Criteria web page (<https://www.fda.gov/STIC>) or on the updates page.

Once a year, FDA is required to compile the new notices published on the Susceptibility Test Interpretive Criteria web page and publish them in the *Federal Register* and provide for public comment (see section 511A(c)(3) of the FD&C Act). This *Federal Register* notice satisfies that requirement. If comments are received, FDA will review them and make updates to the recognized standards or susceptibility test interpretive criteria as needed.

II. Annual Compilation of Notices: Susceptibility Test Interpretive Criteria Web Page

A. *Formatting Changes to the Susceptibility Test Interpretive Criteria Web Page*

On October 4, 2018, FDA updated the format of the Antifungal Susceptibility Test Interpretive Criteria web pages for clarity, in response to stakeholder feedback.

On June 26, 2018, FDA updated the format of the Antibacterial Susceptibility Test Interpretive Criteria web pages for clarity, in response to stakeholder feedback.

B. *Updates to Standards Recognition*

As of October 4, 2018, the following susceptibility test interpretive criteria standards are no longer recognized (for information regarding recognition of methods and quality control standards see Recognized Consensus Standards):

- Clinical and Laboratory Standards Institute (CLSI). Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Fourth Informational Supplement. CLSI document M27-S4 (2012). Clinical and Laboratory Standards Institute, 940 West Valley Rd., Suite 2500, Wayne, PA 19087, USA (CLSI M27-S4).
- Clinical and Laboratory Standards Institute (CLSI). Method for Antifungal Disk Diffusion Susceptibility Testing of Yeasts; Approved Guideline--Second Edition. CLSI

document M44-S3 (2009). Clinical and Laboratory Standards Institute, 950 West Valley Rd., Suite 500, Wayne, PA 19087, USA (CLSI M44-S3).

- Clinical and Laboratory Standards Institute (CLSI). Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Fourth Informational Supplement. CLSI document M27-S3 (2008). Clinical and Laboratory Standards Institute, 940 West Valley Rd., Suite 2500, Wayne, PA 19087, USA (CLSI M27-S3).

As of October 4, 2018, with certain exceptions, FDA recognizes the following standard:

- Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antifungal Susceptibility Testing of Yeasts. 1st ed. CLSI supplement M60 (2017). Clinical and Laboratory Standards Institute, 940 West Valley Rd., Suite 2500, Wayne, PA 19087, USA (CLSI M60).

As of June 26, 2018, the following standard is no longer recognized:

- Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing. 27th ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2017.

As of June 26, 2018, with certain exceptions, FDA recognizes the following standard:

- Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing. 28th ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2018.

Table 1.--Notices of Updates to Recognized or Updated Susceptibility Test Interpretive Criteria by Drug

Drug	Route of Administration	Action Taken	Therapeutic Category	Date
Fluconazole	Injection, Oral	FDA identifies exceptions to the recognized standard for Fluconazole. The term "Susceptible-Dose Dependent" is not recognized pending further clarification of the definition of the term by standards	Antifungal	10/3/18

Drug	Route of Administration	Action Taken	Therapeutic Category	Date
		development organizations.		
Flucytosine	Injection	FDA withdraws recognition of Susceptibility Test Interpretive Criteria for Flucytosine as there are not sufficient clinical or other data to support these criteria.	Antifungal	10/3/18
Itraconazole	Injection, Oral	FDA identifies Susceptibility Test Interpretive Criteria for itraconazole and <i>Candida albicans</i> . The current minimum inhibitory concentration distribution data demonstrates that the sensitivity of <i>C. albicans</i> to itraconazole has not changed over time. Therefore, the in-vitro activity and clinical response data reviewed previously by FDA and described in product labeling continue to support these interpretive criteria for <i>C. albicans</i> .	Antifungal	10/3/18
Omadacycline	Injection, Oral	Added drug to antibacterial susceptibility test interpretive criteria web page. FDA identified susceptibility test interpretive criteria for omadacycline injection.	Antifungal	10/3/18
Bismuth subcitrate potassium, Metronidazole, and Tetracycline hydrochloride	Oral	Added drug to antibacterial susceptibility test interpretive criteria web page. No susceptibility test interpretive criteria recognized or added by FDA.	Antibacterial	2/09/18
Ceftazidime Avibactam	Injection	FDA recognizes M100 standard for <i>Enterobacteriaceae</i> and <i>Pseudomonas aeruginosa</i> .	Antibacterial	6/26/18
Ceftolozane Tazobactam	Injection	FDA recognizes M100 standard for disk diffusion for <i>Enterobacteriaceae</i> .	Antibacterial	6/26/18
Clarithromycin	Oral	FDA recognizes CLSI M45 standard for clarithromycin for <i>Helicobacter pylori</i> .	Antibacterial	2/09/18
Dalbavancin	Injection	FDA recognizes M100 standard for <i>Staphylococcus aureus</i> , <i>Enterococcus</i> spp. (vancomycin-susceptible isolates only), <i>Streptococcus</i> spp β - Hemolytic Group, <i>Streptococcus</i> spp Viridans Group.	Antibacterial	6/26/18
Eravacycline	Injection	Added drug to antibacterial susceptibility test interpretive criteria web page. FDA identified susceptibility test interpretive criteria for eravacycline injection.	Antibacterial	8/28/18
Isoniazid, Pyrazinamide, and Rifampin	Oral	Added drug to antibacterial susceptibility test interpretive criteria web page. No susceptibility test interpretive criteria recognized or added by FDA.	Antibacterial	2/09/18

Drug	Route of Administration	Action Taken	Therapeutic Category	Date
Lansoprazole, Amoxicillin, and Clarithromycin	Oral	Added drug to antibacterial susceptibility test interpretive criteria web page. No susceptibility test interpretive criteria recognized or added by FDA.	Antibacterial	2/09/18
Piperacillin Tazobactam	Injection	FDA recognizes revised M100 standard for anaerobes.	Antibacterial	6/26/18
Plazomicin	Injection	Added drug to antibacterial susceptibility test interpretive criteria web page. FDA identified susceptibility test interpretive criteria for plazomicin injection.	Antibacterial	6/26/18
Rifabutin	Oral	Added drug to antibacterial susceptibility test interpretive criteria web page. No susceptibility test interpretive criteria recognized or added by FDA.	Antibacterial	4/26/18
Rifapentine	Oral	Added drug to antibacterial susceptibility test interpretive criteria web page. No susceptibility test interpretive criteria recognized or added by FDA.	Antibacterial	2/09/18
Rifaximin	Oral	Added drug to antibacterial susceptibility test interpretive criteria web page. No susceptibility test interpretive criteria recognized or added by FDA.	Antibacterial	2/09/18
Tedizolid	Oral, Injection	Due to test performance concerns, FDA withdraws recognition of all disk diffusion interpretive criteria.	Antibacterial	6/26/18

Dated: April 29, 2019.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

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